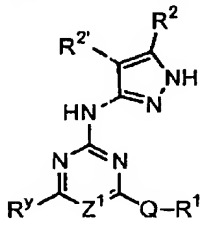
Applicants: David Bebbington, et al.
Application No.: 10/775,699

IN THE CLAIMS:

Please replace all prior versions and listings of claims with the currently amended claims as follows. Please cancel claims 18-19, 24-25, and 30-31, and amend claims 1, 12, 13, and 34.

Claim 1. (Currently amended) A compound of formula II:



II

or a pharmaceutically acceptable salt ~~or prodrug~~ thereof, wherein:

Z^1 is CR^8;

R^y is $Z\text{-}R^{3'}$ or an optionally substituted group selected from C_{1-6} aliphatic, C_{6-10} aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms, or R^y and R^8 are taken together to form a fused, optionally substituted 5-7 membered, unsaturated or partially unsaturated, ring having 0-3 ring heteroatoms selected from nitrogen, oxygen, or sulfur;

Q is selected from $-N(R^4)-$, -O-, –S-, or $-CH(R^6)-$;

R^1 is T-(Ring D);

Ring D is a 6-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms selected from nitrogen, oxygen or sulfur, wherein each substitutable ring carbon of Ring D is independently substituted by oxo, $T\text{-}R^5$, or $V\text{-}Z\text{-}R^5$, and each substitutable ring nitrogen of Ring D is independently substituted by $-R^4$;

T is a valence bond or a C_{1-4} alkylidene chain, wherein when Q is $-CH(R^6)-$, a methylene unit of said C_{1-4} alkylidene chain is optionally replaced by -O-, -S-, $-N(R^4)-$, -CO-, -CONH-, -NHCO-, $-SO_2-$, $-SO_2NH-$, $-NHSO_2-$, $-CO_2-$, -OC(O)-, -OC(O)NH-, or $-NHCO_2-$;

Z is a C_{1-4} alkylidene chain;

~~L is $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-N(R^6)SO_2-$, $-SO_2N(R^6)-$, $-N(R^6)-$, $-CO-$, $-CO_2-$, $-N(R^6)CO-$, $-N(R^6)C(O)O-$, $-N(R^6)CON(R^6)-$, $-N(R^6)SO_2N(R^6)-$, $-N(R^6)N(R^6)-$, $-C(O)N(R^6)-$, $-OC(O)N(R^6)-$, $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$,~~

Applicants: David Bebbington, et al.
Application No.: 10/775,699

~~$-C(R^6)_2N(R^6)-$, $-C(R^6)_2N(R^6)C(O)-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, or $-C(R^6)_2N(R^6)CON(R^6)-$;~~

R^2 and $R^{2'}$ are independently selected from -R, -T-W-R^6, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a fused, 5-8 membered, unsaturated or partially unsaturated, ring having 0-3 ring heteroatoms selected from nitrogen, oxygen, or sulfur, wherein each substitutable ring carbon of said fused ring formed by R^2 and $R^{2'}$ is independently substituted by halo, oxo, -CN, $-NO_2$, $-R^7$, or -V-R^6, and each substitutable ring nitrogen of said ring formed by R^2 and $R^{2'}$ is independently substituted by R^4;

$R^{3'}$ is selected from -halo, -OR, -C(=O)R, $-CO_2R$, -COCOR, $-COCH_2COR$, $-NO_2$, -CN, -S(O)R, $-S(O)_2R$, -SR, $-N(R^4)_2$, $-CON(R^7)_2$, $-SO_2N(R^7)_2$, -OC(=O)R, $-N(R^7)COR$, $-N(R^7)CO_2(C_{1-6}$ aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^7)CON(R^7)_2$, $-N(R^7)SO_2N(R^7)_2$, $-N(R^4)SO_2R$, $-OC(=O)N(R^7)_2$, or an optionally substituted group selected from C_{1-6} aliphatic, C_{6-10} aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms;

each R is independently selected from hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, C_{6-10} aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms;

each R^4 is independently selected from $-R^7$, $-COR^7$, $-CO_2$(optionally substituted C_{1-6} aliphatic), $-CON(R^7)_2$, or $-SO_2R^7$;

each R^5 is independently selected from -R, halo, -OR, -C(=O)R, $-CO_2R$, -COCOR, $-NO_2$, -CN, -S(O)R, $-SO_2R$, -SR, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, -OC(=O)R, $-N(R^4)COR$, $-N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$;

V is $-O-$, -S-, -SO-, $-SO_2-$, $-N(R^6)SO_2-$, $-SO_2N(R^6)-$, $-N(R^6)-$, -CO-, $-CO_2-$, $-N(R^6)CO-$, $-N(R^6)C(O)O-$, $-N(R^6)CON(R^6)-$, $-N(R^6)SO_2N(R^6)-$, $-N(R^6)N(R^6)-$, $-C(O)N(R^6)-$, $-OC(O)N(R^6)-$, $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$, $-C(R^6)_2N(R^6)-$, $-C(R^6)_2N(R^6)C(O)-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, or $-C(R^6)_2N(R^6)CON(R^6)-$;

W is $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$, $-C(R^6)_2N(R^6)-$, -CO-, $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)OC(O)N(R^6)-$, $-C(R^6)_2N(R^6)CO-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, $-C(R^6)_2N(R^6)CON(R^6)-$, or $-CON(R^6)-$;

Applicants: David Bebbington, et al.
Application No.: 10/775,699

each R^6 is independently selected from hydrogen or an optionally substituted C_{1-4} aliphatic group, or two R^6 groups on the same nitrogen atom are taken together with the nitrogen atom to form a 5-6 membered heterocyclyl or heteroaryl ring;

each R^7 is independently selected from hydrogen or an optionally substituted C_{1-6} aliphatic group, or two R^7 on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring; and

R^8 is selected from -R, halo, -OR, -C(=O)R, $-CO_2R$, -COCOR, $-NO_2$, -CN, -S(O)R, $-SO_2R$, -SR, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, $-OC(=O)R$, $-N(R^4)COR$, $-N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$; provided that when Q is -NH- and R^y and R^8 are taken together, R^1 is other than pyrazol-3-yl or a bicyclic ring system containing said pyrazol-3-yl ring.

Claims 2-7. (Canceled).

Claims 8. (Previously presented) The compound according to claim 1, wherein said compound has one or more features selected from the group consisting of:

(a) R^y is $Z\text{-}R^{3'}$ or an optionally substituted group selected from C_{1-6} aliphatic, 5-6 membered heterocyclyl, phenyl, or 5-6 membered heteroaryl, wherein Z is a methylene and $R^{3'}$ is $-N(R^4)_2$, -OR, or an optionally substituted group selected from C_{1-6} aliphatic, C_{6-10} aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms;

(b) R^1 is T-(Ring D), wherein T is a valence bond or a methylene unit;

(c) Ring D is a a ~~5~~ 6-7 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(d) R^2 is –R or –T-W-R^6 and $R^{2'}$ is hydrogen, or R^2 and $R^{2'}$ are taken together to form an optionally substituted benzo ring.

Claim 9. (Previously presented) The compound according to claim 8, wherein:

(a) R^y is $Z\text{-}R^{3'}$ or an optionally substituted group selected from C_{1-6} aliphatic, 5-6 membered heterocyclyl, phenyl, or 5-6 membered heteroaryl, wherein Z is a methylene and $R^{3'}$ is $-N(R^4)_2$, -OR, or an optionally substituted group selected

from C_{1-6} aliphatic, C_{6-10} aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms;

(b) R^1 is T-(Ring D), wherein T is a valence bond or a methylene unit;

(c) Ring D is a 6-7 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(d) R^2 is –R or –T-W-R^6 and $R^{2'}$ is hydrogen, or R^2 and $R^{2'}$ are taken together to form an optionally substituted benzo ring.

Claims 10. (Previously presented) The compound according to claim 8, wherein said compound has one or more features selected from the group consisting of:

(a) R^y is an optionally substituted group selected from C_{1-6} aliphatic, 5-6 membered heterocyclyl, phenyl, or 5-6 membered heteroaryl;

(b) R^1 is T-(Ring D), wherein T is a valence bond, and Q is -S-, -NH-, or -CH_2-;

(c) Ring D is a 6 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(d) R^2 is –R and $R^{2'}$ is hydrogen, wherein R is selected from hydrogen, C_{1-6} aliphatic, phenyl, a 5-6 membered heteroaryl ring, or a 5-6 membered heterocyclic ring.

Claim 11. (Previously presented) The compound according to claim 10, wherein:

(a) R^y is an optionally substituted group selected from C_{1-6} aliphatic, 5-6 membered heterocyclyl, phenyl, or 5-6 membered heteroaryl;

(b) R^1 is T-(Ring D), wherein T is a valence bond, and Q is -S-, -NH-, or -CH_2-;

(c) Ring D is a 6 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(d) R^2 is –R and $R^{2'}$ is hydrogen, wherein R is selected from hydrogen, C_{1-6} aliphatic, phenyl, a 5-6 membered heteroaryl ring, or a 5-6 membered heterocyclic ring.

Claim 12. (Currently amended) The compound according to claim 10, wherein said compound has one or more features selected from the group consisting of:

(a) R^y is selected from 2-pyridyl, 4-pyridyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, methyl, ethyl, cyclopropyl, isopropyl, t-butyl, alkoxyalkylamino, alkoxyalkyl, alkyl- or dialkylamino, alkyl- or dialkylaminoalkoxy, acetamido, optionally substituted phenyl, or methoxymethyl, or R^y and R^8 are taken

together to form a 5-6 membered unsaturated or partially unsaturated ring having 0-2 heteroatoms selected from nitrogen, oxygen, or sulfur;

(b) R^1 is T-(Ring D), wherein T is a valence bond and Ring D is a 6 membered aryl or heteroaryl ring, wherein Ring D is optionally substituted with one to two groups selected from -halo, -CN, $-NO_2$, $-N(R^4)_2$, optionally substituted C_{1-6} aliphatic group, -OR, $-CO_2R$, $-CONH(R^4)$, $-N(R^4)COR$, $-N(R^4)SO_2R$, $-N(R^6)COCH_2CH_2N(R^4)_2$, or $-N(R^6)COCH_2CH_2CH_2N(R^4)_2$, and Q is -S- or -NH-; and

(c) R^2 is hydrogen or a substituted or unsubstituted C_{1-6} aliphatic, and ~~L is O, S, or NH.~~

Claim 13. (Currently amended) The compound according to claim 12, wherein:

(a) R^y is selected from 2-pyridyl, 4-pyridyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, methyl, ethyl, cyclopropyl, isopropyl, t-butyl, alkoxyalkylamino, alkoxyalkyl, alkyl- or dialkylamino, alkyl- or dialkylaminoalkoxy, acetamido, optionally substituted phenyl, or methoxymethyl, or R^y and R^8 are taken together to form a 5-6 membered unsaturated or partially unsaturated ring having 0-2 heteroatoms selected from nitrogen, oxygen, or sulfur;

(b) R^1 is T-(Ring D), wherein T is a valence bond and Ring D is a 6 membered aryl or heteroaryl ring, wherein Ring D is optionally substituted with one to two groups selected from -halo, -CN, $-NO_2$, $-N(R^4)_2$, optionally substituted C_{1-6} aliphatic group, -OR, $-CO_2R$, $-CONH(R^4)$, $-N(R^4)COR$, $-N(R^4)SO_2R$, $-N(R^6)COCH_2CH_2N(R^4)_2$, or $-N(R^6)COCH_2CH_2CH_2N(R^4)_2$, and Q is -S- or -NH-; and

(c) R^2 is hydrogen or a substituted or unsubstituted C_{1-6} aliphatic, and ~~L is O, S, or NH.~~

Claim14. (Previously presented) A compound selected from the group consisting of:

6-Benzyl-*N*^{4}-(1*H*-indazol-6-yl)-*N*^{2}-(5-methyl-1*H*-pyrazol-3-yl)-pyrimidine-2,4-diamine;

6-Methyl-*N*^{2}-(5-methyl-1*H*-pyrazol-3-yl)-*N*^{4}-pyridine-3-ylmethyl-pyrimidine-2,4-diamine;

N-(4-{2-(5-Methyl-1*H*-pyrazol-3-ylamino)-6-[(pyridin-3-ylmethyl)-amino]-pyrimidin-4-ylamino}-phenyl)-methanesulfonamide;

Applicants: David Bebbington, et al.
Application No.: 10/775,699

N^2-(5-Cyclopropyl-1*H*-pyrazol-3-yl)-N^4-(2-methoxy-ethyl)-6-(thiophen-2-ylmethylsulfanyl)-pyrimidine-2,4-diamine;

[4-(Benzothiazol-6-ylsulfanyl)-6-(3-dimethylamino-propoxy)-pyrimidin-2-yl]-(5-cyclopropyl-1*H*-pyrazol-3-yl)-amine;

N-(4-[2-(5-Cyclopropyl-1*H*-pyrazol-3-ylamino)-6-(1-methyl-piperidin-4-yloxy)-pyrimidin-4-ylsulfanyl]-phenyl}-acetamide;

N-{4-[2-(5-Methyl-1*H*-pyrazol-3-ylamino)-quinazolin-4-ylsulfanyl]-phenyl}-acetamide;

[4-(Benzothiazol-6-ylsulfanyl)-quinazolin-2-yl-(5-methyl-1*H*-pyrazol-3-yl)-amine;

{4-[2-(5-Cyclopropyl-1*H*-pyrazol-3-ylamino)-quinazolin-4-yloxy]-phenyl}-acetonitrile;

(5-Cyclopropyl-1*H*-pyrazol-3-yl)-[4-(3-methoxy-benzyl)-quinazolin-2-yl]-amine;

N^2-(1*H*-Indazol-6-yl)-N^4-pyridin-3-ylmethyl-quinazoline-2,4-diamine; and

(4-(Benzyloxy-quinazolin-2-yl-(1*H*-indazol-3-yl)-amine.

Claim15. (Original) A composition comprising a compound according to any one of claims 1-14, and a pharmaceutically acceptable carrier.

Claim 16. (Original) The composition according to claim 15, further comprising an additional therapeutic agent.

Claims 17-34. (Canceled)